

WE CLAIM

Sure C1 > 1. A method for providing a β_2 -adrenergic receptor (β_2 AR) to airway epithelial cells, airway smooth muscle cells, blood vessel endothelial cells, blood vessel smooth muscle cells or a combination thereof, of a human subject comprising:

administering to at least one cell type selected from the group consisting of airway epithelial cells, airway smooth muscle cells, blood vessel endothelial cells, and blood vessel smooth muscle cells of a human subject, a first composition comprising a vector comprising a DNA sequence encoding a β_2 AR operably linked to a promoter that is functional in at least one of said cells of said subject, under conditions whereby the DNA sequence encoding said β_2 AR is expressed in at least one of said cells.

2. The method of claim 1, wherein said DNA sequence encodes a β_2 AR that is modified as compared to the native β_2 AR.

Sure C2 > 3. The method of claim 1, wherein said promoter is an inducible promoter, and said method further comprises

administering a second composition comprising a hormone or pharmacological agent that induces said promoter to express said β_2 AR in at least one of said cells.

4. The method of claim 1, wherein said method further comprises:

administering a second composition comprising at least one β_2 -adrenergic agonist to said cells of said subject.

5. The method of claim 4, wherein said promoter is an inducible promoter, said method further comprises:

administering a third composition comprising a hormone or pharmacological agent that induces said promoter to express said β_2 AR in at least one of said cells.

6. A host cell transfected by a vector comprising a DNA sequence encoding a β_2 AR operably linked to a promoter that is functional in said cell.

7. The method of claim 6, wherein said DNA sequence encodes a β_2 AR that is modified as compared to the native β_2 AR.

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8. A method of treating a human subject having airway or vascular disease comprising:

administering to at least one cell type selected from the group consisting of airway epithelial cells, airway smooth muscle cells, blood vessel endothelial cells, and blood vessel smooth muscle cells, a first composition comprising a vector comprising a DNA sequence encoding a β_2 AR operably linked to a promoter that is functional in at least one of said cells of said subject, under conditions whereby the DNA sequence encoding said β_2 AR is expressed in at least one of said cells; and

administering a second composition comprising at least one β_2 -adrenergic agonist into said cells of said subject.

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9. The method of claim 1 wherein said epithelial cell is an airway epithelial cell.

10. The method of claim 1, wherein said vector is a viral vector or a non-viral vector.

11. The method of claim 10, wherein said viral vector is selected from the group consisting of an adeno-associated vector (AAV), an adenovirus vector and a retrovirus vector.

12. The method of claim 10, wherein said non-viral vector is a liposome.

13. The method of claim 10, wherein said promoter is selected from the group consisting of a viral vector promoter and a mammalian cell specific promoter.

14. The method of claim 13, wherein said mammalian cell specific promoter is selected from the group consisting of an epithelial cell specific promoter, an endothelial cell specific promoter and a smooth muscle cell specific promoter.

15. The method of claim 13, wherein said viral vector promoter is a cytomegalovirus (CMV) promoter or an adeno-associated vector (AAV) promoter.

16. The method of claim 15, wherein said vector is an AAV vector and said promoter is a CMV promoter.

17. The method of claim 13, wherein said promoter is an inducible promoter.

Suf C4 18. The method of claim 17, wherein said method further comprises:
administering a composition comprising a hormone or pharmacological agent
that induces said promoter to express said β_2 AR in at least one of said cells.

19. The method of claim 1, wherein said vector further comprises at least one
enhancer element or regulatory element.

Suf C5 20. The method of claim 1, wherein said first composition further comprises a
pharmaceutically acceptable carrier for aerosol delivery or for intravenous delivery.

21. The method of claim 4, wherein said second composition is administered
sequentially after the administration of said first composition.

22. The method of claim 8, wherein said second composition is administered
sequentially after the administration of said first composition.

23. The method of claim 3, wherein said first and second compositions further
comprise a pharmaceutically acceptable carrier for aerosol delivery.

24. The method of claim 4, wherein said first and second compositions further
comprise a pharmaceutically acceptable carrier for aerosol delivery.

25. The method of claim 5, wherein said first, said second and said third
compositions further comprise a pharmaceutically acceptable carrier for aerosol delivery.

26. The method of claim 8, wherein said first and second compositions further
comprise a pharmaceutically acceptable carrier for aerosol delivery.

27. The method of claim 8, wherein said DNA sequence encodes a β_2 AR that is
modified as compared to the native β_2 AR.

28. The method of claim 2, wherein said modified β_2 AR possesses at least one
property selected from the group consisting of increased responsiveness to β_2 AR agonists,
increased affinity to β_2 -adrenergic agonists, and capability to increase the potency of β_2 AR

agonists to stimulate downstream signal transduction pathways, as compared to the native β_2 AR.

29. The method of claim 28, wherein said modified β_2 AR is modified from the native β_2 AR by the deletion of amino acids, substitution of amino acids, replacement of amino acids or a combination thereof.

Jfj Cle 30. A pharmaceutical composition comprising a vector comprising a DNA sequence encoding a β_2 AR operably linked to a promoter that is functional in at least one cell of the airways or blood vessels of a human subject, wherein said cell is selected from the group consisting of an airway epithelial cells, airway smooth muscle cells, blood vessel endothelial cells and blood vessel smooth muscle cells; and a pharmaceutically acceptable carrier.

31. The pharmaceutical composition of claim 30, wherein said DNA sequence encodes a β_2 AR that is modified as compared to the native β_2 AR.

Jfj 1 32. The pharmaceutical composition of claim 30, wherein said pharmaceutical composition is suitable for aerosol delivery or intravenous delivery.

33. A kit for the treatment of a human subject having airway or vascular disease comprising:

a first pharmaceutical composition comprising a vector comprising a DNA sequence encoding a β_2 AR operably linked to a promoter that is functional in at least one cell of the airways or blood vessels of a human subject, wherein said cell is selected from the group consisting of an airway epithelial cells, airway smooth muscle cells, blood vessel endothelial cells and blood vessel smooth muscle cells; and a pharmaceutically acceptable carrier; and

a second pharmaceutical composition comprising at least one β_2 -adrenergic agonist and a pharmaceutically acceptable carrier.

34. The kit of claim 33, wherein said β_2 AR is modified as compared to the native β_2 AR.

SAC 8 > 35. The kit of claim 33, wherein said promoter is an inducible promoter, said kit further comprises:

a third pharmaceutical composition comprising a hormone or pharmacological agent that induces said promoter to express said β_2 AR in at least one of said cells

36. The kit of claim 33, wherein said kit is for the treatment of said subject with an airway disease and said pharmaceutically acceptable carrier of said first and said second pharmaceutical composition are suitable for aerosol delivery.

37. The kit of claim 33, wherein said kit is for the treatment of said subject with a vascular disease and said pharmaceutically acceptable carriers of said first and second pharmaceutical composition are suitable for intravenous delivery.

SAC 9 > 38. A kit for the treatment of a human subject having airway or vascular disease comprising:

a first pharmaceutical composition comprising a vector comprising a DNA sequence encoding a β_2 AR operably linked to a promoter that is functional in at least one cell of the airways or blood vessels of a human subject, wherein said cell is selected from the group consisting of an airway epithelial cells, airway smooth muscle cells, blood vessel endothelial cells and blood vessel smooth muscle cells; and a pharmaceutically acceptable carrier; and

a second pharmaceutical composition comprising a hormone or pharmacological agent that induces said promoter to express said β_2 AR in at least one of said cells.

39. A kit for the treatment of a human subject having airway or vascular disease comprising:

a first pharmaceutical composition comprising at least one β_2 -adrenergic agonist and a pharmaceutically acceptable carrier, and

a second pharmaceutical composition comprising a hormone or pharmacological agent that induces a promoter that is functional in at least one cell of the airways or blood vessels of a human subject, wherein said cell is selected from the group consisting of an airway epithelial cells, airway smooth muscle cells, blood vessel

endothelial cells and blood vessel smooth muscle cells, said promoter to direct the expression of a β_2 AR in at least one of said cells.

40. An *in vitro* method of expressing the β_2 AR gene comprising:
transducing at least one mammalian cell with a recombinant vector that carries the nucleic acid sequence encoding the native β_2 AR or a modified β_2 AR, and expressing said β_2 AR gene in said cell.
41. The method of claim 40, wherein said method further comprises contacting said transduced cell with a pharmacological compound and evaluating the effect of the compound on the expression of said β_2 AR gene.
42. The method of claim 41, wherein said mammalian cell is an epithelial cell.
43. The method of claim 41, wherein said vector is an AAV vector.

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